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(54) Title: A BLOOD DETECTION COMPOSITION

(57) Abstract

The present invention relates to chemical compositions capable of blood detection which provide a visual signal in form of a color change. The compositions comprise an oxidisable color indicator and a peroxide or a per–acid and a stabilizer which is selected from cyclo–dextrin, nitrone or combinations thereof. These compositions are useful as ingredients of sanitary articles for the prediction of the approach of menstruation by providing a visual signal due to the detection of blood prior to the blood being contained in these articles in visually discernible quantities.

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A BLOOD DETECTION COMPOSITION

FIELD OF THE INVENTION

The present invention relates to chemical compositions capable of blood detection which provide a visual signal in form of a color change. The compositions comprise an oxidisable color indicator and a peroxide or a per-acid and a stabilizer which is selected from cyclo-dextrin, nitrone or combinations thereof. These compositions are useful as ingredients of sanitary articles for the prediction of the approach of menstruation by providing a visual signal due to the detection of blood prior to the blood being contained in these articles in visually discernible quantities.

BACKGROUND OF THE INVENTION

Today, disposable articles, such as diapers, adult incontinence briefs, sanitary napkins, panty liners, interlabial devises and tampons, are widely used in feminine protection, infant and toddler care and in the care of incontinent adults as a means of containing, isolating and disposing of bodily wastes. These articles have generally replaced reusable, washable cloth garments as the preferred means for these applications because of their convenience and reliability. The disposable articles respond to a discharge event by absorbing or containing bodily wastes deposited on the article. Some disposable articles comprise a chemically reactive means to detect and signal various substances in the wearer's waste(s). However, none of these specifically detect or predict when a menstruation-related discharge event is about to occur and signal to the wearer or caregiver that occurrence.

The so far un-met consumer need of women which is targeted by the present invention is the desire to gain more information about the expected timing of their menstruation. More generally it is well established that women would like to know more about and monitor their bodily condition as relates to the status of their menstruation cycle as well as a pre-warning to any kind of related disorder advancing. On the other hand the compositions used in this context need to satisfy the highest standards of safety for the user as well as for the environment.

A lot of disclosure exists on general diagnostic aspects relating to female menstruation cycle and genital/urinary tract related information. However, none of the references cited in the following does provide specific teaching to the present invention.

US 5,217,444 to Schönfeld et. al., published June 8, 1993 discloses absorbent pads such as tampons comprising a pH indicator material to indicate the acidity or alkalinity of a liquid by a color change. The pH indictor is intended to be wetted by vaginal secretions which are absorbed by the pad. Depending on the pH this will provide an indication of the health condition of the women's vaginal tract.

US 5,468,236 to Everhart et. al., published November 21, 1995 discloses a disposable absorbent product incorporating a chemically reactive substance which can provide visual indication of a chemical component in absorbed liquid such as vaginal discharges. The patent is un-specific as to its particular purpose but exemplifies a disposable diaper in which a glucose indicating gel can be applied to the topsheet or the absorbent core. In a second example the chemical compound to be detected is a nitrate as indicator of urinary tract infections by GRAM negative bacteria. In particular Everhart provides for a reaction which is endpoint stable due to a catalytic sequence such that further liquid absorption will not alter the indication.

US 4,231,370 to Morz et. al., published November 4, 1980 discloses disposable diapers with a pH sensitive wetness indicator in a solid adhesive matrix.

US 5,823,953 to Richards et. al., published October 20, 1998 relates to a self diagnostic system for yeast or non-yeast related vaginal infections in the form of a catamenial pad or panty liner with detachable, color indicating pH strip mounted on the topsheet. The pH indicator identifies if the pH of the absorbed liquid is above or below a thresh hold value of 4.5 and is indented to allow health care decisions without a physician in respect to treating a yeast or a non-yeast vaginal infection.

WO 97/43955 to Buck et. al., published November 27, 1997 discloses a kit for home use for collecting vaginal fluid and exfoliated vaginal cells in menstrual fluid for diagnostic purposes. The fluid or cells are collected in an absorbent interlabial pad or in a pad which is placed inside an apertured housing which is placed inter vaginally for collecting fluid. The fluid can afterwards be used for diagnostic purposes as desirable.

EP 704 195, to Echeveria, published April 3, 1996 discloses a menstrual detector which comprises a sanitary napkin or panty liner including a chemical compound which provides a cooling reaction upon liquid absorption as indicator of the start of menstruation in order to allow the wearer sufficient time to replace the indicating absorbent article by a full size and full capacity sanitary napkin or tampon.

Of course, many indicators as such are known and are usually independent of the source of the liquid of which analysis is desired. For example, EP 386 562 to Ismael et. al., published September 12, 1990 discloses a dry enzyme test composition with a color indicator result. Similarly, WO 90/06511 to Buck et. al.,

published June 14, 1990 discloses a stabilized indicator to determine the presence of an analyte in a liquid sample. Similarly, WO 89/11643 to Bouse et al, published November 30, 1989 discloses an indictor composition designed to increase the range of analyte concentration which can be analyzed.

EP 124 215 and EP 124 214 both to Oksman et al, published November 7, 1984 relate to wipe indicators for occult blood particular useful to analyze the presence of blood in feces. Similarly, EP 93595, to Wells, published November 9, 1983 relates to a dry diagnostic aid for use in an one-step determination of hemoglobin, especially in occult blood in feces.

EP 113 896 to Rothe, published July 25, 1984 relates to a chemical testing strip in which a test reagent is provided on a plastic film strip for quantitative evaluation. This patent exemplifies blood and glucose testing.

EP 101 980 and EP 101 979, both to Roy, published March 7, 1984 relate to the determination of dehydrogenase for the purpose of rapid clinical analysis and diagnosis. In the later case it is said that the carrier can be a tampon containing cellulose fibers.

In addition many publications in the medical field relating to pathological conditions of the female genital and urinary organs including methods of detecting and healing them have been published.

SUMMARY OF THE INVENTION

The present invention relates to a stabilized detection composition for providing a visual signal of the detection of blood in liquids which blood is not discernible by normal visual inspection by the human eye. According to the invention the blood is generally contained in bodily fluids of mammalian origin or can be in the form of an aqueous solution. The blood detection composition comprises an

oxidisable color indicator and an oxidant such as peroxide or a per-acid which is stabilized by a component selected from cyclo-dextrin or nitrone or combinations thereof.

In a preferred embodiment of the present invention the oxidisable color indicator is selected from the group consisting of Gum Guaiac, tetra-methyl benzidine or combinations thereof. Also preferred are compositions in which the oxidizing reactant is selected from hydro-peroxides, epta-phtalimido-peroxy-hexanoic acid or combinations thereof.

The composition can be contained in any kind of article but is preferably comprised in absorbent sanitary articles for women which provide a visual blood detection of a quantity of blood in vaginal discharges deposited on the article which is not discernible. The article can be of a layered construction, each layer having a wearer and a garment facing surface. In general the article comprises a liquid permeable topsheet on the wearer facing surface, a liquid barrier backsheet on the garment facing surface, an absorbent core sandwiched between the topsheet and the backsheet. According to the present invention the article is preferably a sanitary napkin or panty liner, especially a thin panty liner with less than 3 mm thickness and most preferred a panty liner which is suitable to be worn in a string undergarment and has a generally triangular shape.

According to a preferred embodiment of the present invention stabilizing component is provided by cyclo-dextrin or nitrone or combinations thereof. The composition can preferably be provided in liquid form, such as in an organic solvent. When applying the composition to an article it is preferred to provide it in a liquid form, more preferably as a solution in an organic carrier which evaporates after the composition has been applied. Application can be done by coating or preferably by spraying. Alternatively the composition can be provided in particulate form. In order to ensure that the composition or its components are dissolved the presence of a tensioactive component such as a surfactant or polyethylene glycol is also preferred. If the tensioactive material is an organic

material it can also be used as the carrier for the composition. In such a case the evaporation of the organic carrier then becomes obsolete.

It is within the scope of the present invention to supplement the blood detector by additional menstruation related detectors such as additional bio-chemical or electro-chemical or chemical detection means suitable to create a separate, strengthened or modified visual signal. Preferably such an additional detection means comprises a pH indicator or a progesterone hormone or estrogen hormone indicator or combinations thereof.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

As used herein, the term "absorbent article" refers to devices which absorb and contain body exudates, and more specifically, refers to devices which are placed against or in proximity to the body of the wearer to absorb and contain the various exudates discharged from the body. The term "disposable" is used herein to describe absorbent articles which generally are not intended to be laundered or otherwise restored or reused as an absorbent article (i.e., they are intended to be discarded after a single use). As used herein, the term "joined" encompasses configurations whereby an element is directly secured to another element by affixing the element directly to the other element, and configurations whereby an element is indirectly secured to another element by affixing the element to intermediate member(s) which in turn are affixed to the other element. A "unitary" absorbent article refers to absorbent articles which are formed of separate parts united together to form a coordinated entity so that they do not require separate manipulative parts like a separate holder and liner. A preferred embodiment of an absorbent article is a unitary disposable sanitary napkin or panty liner, however also disposable incontinence briefs, incontinence undergarments,

absorbent inserts, tampons and interlabial absorbent articles can benefit from the present invention if used during the period prior to menstruation.

An absorbent article, according to the present invention is conventionally constructed of three main elements: The topsheet, facing the user of the article during use and being liquid pervious in order to allow liquids to pass into the article; the backsheet, providing a liquid containment such that absorbed liquid does not leak through the article, this backsheet conventionally provides the garment facing surface of the article; and the absorbent core sandwiched between the topsheet and the backsheet and providing the absorbent capacity of the article to acquire and retain liquid which has entered the article through the topsheet.

Many absorbent articles and constructions are known in the art and have been described in ample detail over time. All of such materials are useful in the context of the present invention, provided they do not interfere with blood detection composition. In the following only those examples, which are particularly beneficial for the use in preferred absorbent articles according to the present invention are mentioned. Those skilled in the art will readily be able to identify alternative materials which can also be used and which maybe particularly desirable in the context of menstruation predicting absorbent articles according to the present invention.

Topsheet

In general the topsheet is compliant, flexible, soft feeling and non-irritating to the wearer's skin. The topsheet preferably also can have elastic characteristics allowing it to stretch in one or two directions. As used herein, the term "flexible" refers to materials that are compliant and will readily conform to the general shape and contours of the human body.

The topsheet can be made from a nonwoven or woven material or a film which has been rendered liquid pervious by aperturing. The topsheet can also be provided as a composite material or be comprised of more than a single layer, e.g. it can have a secondary topsheet or flow control layer. Such films and nonwovens or wovens can be made for example from polymers such as polyethylene or polypropylene compositions. The topsheet can be provided from a transparent (free of color filler) or translucent material (having less than 15%, i.e. about half of the conventional quantity of color filler).

Backsheet

In general the backsheet is compliant, flexible and soft feeling. The backsheet prevents the exudes absorbed and contained in the absorbent core from wetting clothes that contact the absorbent article such as undergarments. Preferably the backsheet is impervious to liquids (e.g., menses, sweat and/or urine). It can be manufactured from a thin plastic film, although other flexible liquid impervious materials can also be used. As used herein, the term "flexible" refers to materials that are compliant and will readily conform to the general shape and contours of the human body. The backsheet preferably also can have elastic characteristics allowing it to stretch in one or two directions.

The backsheet can comprise a woven or nonwoven material, polymeric films such as thermoplastic films of polyethylene or polypropylene, or composite materials such as a film-coated nonwoven material or fiber coated film. Conventionally absorbent articles comprise a backsheet of a polyethylene film having a thickness of from about 0.012 mm to about 0.051 mm, which can be impervious or rendered micro-porous by use of an inert filler and subsequent mechanical stretching.

The backsheet is preferably breathable, i.e. allows the transmission of water vapor, or even more preferable the transmission of air, however without

sacrificing its main purpose to provide leakage protection for absorbed liquids. The backsheet can also comprise more than one breathable layer so as to replace a single breathable backsheet layer by at least 2 or 3 layers of a different or the same material. In particular two breathable layers, in which e.g. the one providing the wearer facing surface is a formed, apertured film with a three dimensional structure and e.g. the other, garment facing layer is a non-woven composite of melt-blown and spun-bonded fibers, are preferred breathable backsheet constructions. As with the topsheet the backsheet can be provided from a transparent or translucent material which would allow easier inspection of detectors inside the article.

Absorbent core

Conventionally the absorbent core can be a single entity or comprise several layers. It can include the following components: (a) optionally a primary fluid distribution layer; (b) optionally a secondary fluid distribution layer; (c) a fluid storage layer; (d) optionally a fibrous layer underlying the storage layer; and (e) other optional components.

a. Primary Fluid Distribution Layer

One optional component of the absorbent core according to the present invention is the primary fluid distribution layer. This primary distribution layer typically underlies the topsheet (if present) and is in fluid communication therewith. The primary distribution layer acquires body fluid for ultimate distribution to the storage layer. This transfer of fluid through the primary distribution layer occurs mainly in the thickness, but may also provide distribution along the longitudinal and transverse directions of the thong liner.

b. Optional Secondary Fluid Distribution Layer

Also optional according to the present invention is a secondary fluid distribution layer. This secondary distribution layer typically underlies the primary distribution layer and is in fluid communication therewith. The purpose of this secondary distribution layer is to readily acquire bodily fluid from the primary distribution layer and distribute it along the longitudinal and transverse directions of the thong liner before transfer to the underlying storage layer. This helps the fluid capacity of the underlying storage layer to be fully utilized.

c. Fluid Storage Layer

Positioned in fluid communication with, and typically underlying the primary or secondary distribution layers, is a fluid storage layer. It comprises preferably but not necessarily super-absorbent gelling materials usually referred to as "hydrogels," "superabsorbent" "hydrocolloid" materials. Absorbent gelling materials are those materials that, upon contact with aqueous fluids, especially body fluids, imbibes such fluids and thus form hydrogels. These absorbent gelling materials are typically capable of absorbing large quantities of aqueous body fluids, and are further capable of retaining such absorbed fluids under moderate pressures. In the prior art these absorbent gelling materials are typically in a granular form of discrete, non-fibrous particles. However, according to the present invention these super-absorbent gelling materials can also be provided in non-granular form, preferably in a fibrous form. If no absorbent gelling materials are provided then the storage layer can be provided by the material conventionally used as carrier material disclosed below.

In the fluid storage layer these absorbent gelling materials can be dispersed homogeneously or non-homogeneously in a suitable fibrous matrix also referred to as carrier. Suitable carriers include cellulose fibers, in the form of fluff or tissues, such as is conventionally utilized in absorbent cores. Modified cellulose fibers such as the stiffened cellulose fibers or viscose fibers can also be used. Synthetic fibers can also be used and include those made of cellulose acetate,

polyvinyl fluoride, polyvinylidene chloride, acrylics (such as Orlon), polyvinyl acetate, non-soluble polyvinyl alcohol, polyethylene, polypropylene, polyamides (such as nylon), polyesters, bi-component fibers, tri-component fibers, mixtures thereof and the like. Preferred synthetic and man-made fibers have a denier of from about 3 denier per filament to about 25 denier per filament, more preferably from about 5 denier per filament to about 16 denier per filament. The carrier fibers can be provided as carded, spun-bonded, melt-blown, wet-laid, air-laid substrates or combination of such lay down methods or combinations of such substrates.

Also preferably, the fiber surfaces are hydrophilic or are treated to be hydrophilic. A storage layer can also include filler materials, such as Perlite, diatomaceous earth, Vermiculite, etc., that lower rewet problems. Further the storage layer may comprise a binder including but not limited to Latex binders which can be sprayed as an aqueous solution onto the surface of the storage layer prior to curing.

If the absorbent gelling materials are dispersed non-homogeneously in a fibrous matrix, the storage layer can be locally homogeneous, i.e. have a distribution gradient in one or several directions within the dimensions of the storage layer. Non-homogeneous distribution thus includes e.g. laminates of the fibrous carriers enclosing the absorbent gelling materials or regions in which the absorbent gelling material has a different concentration relative to other regions.

If absorbent gelling material is present the storage layer preferably comprises from 5% to 95% absorbent gelling materials, preferably from 5% to 50%, most preferably from 8% to 35%, absorbent gelling materials. Further the storage layer can comprise from 5% to 95% carrier fibers, preferably from 95% to 50%, most preferably from 92% to 65% carrier fibers.

Suitable absorbent gelling materials for use herein will most often comprise a substantially water-insoluble, slightly crosslinked, partially neutralized, polymeric gelling material. This material forms a hydrogel upon contact with water. Such polymer materials can be prepared from polymerizable, unsaturated, acid-containing monomers. Suitable unsaturated acidic monomers for use in preparing the polymeric absorbent gelling material used in this invention include those listed in U.S. Patent 4,654,039 (Brandt et al), issued March 31, 1987, and reissued as RE 32,649 on April 19, 1988. Preferred monomers include acrylic acid, methacrylic acid, and 2-acrylamido-2-methyl propane sulfonic acid. Acrylic acid itself is especially preferred for preparation of the super-absorbent material, it also has a 'natural' transparency which is not optimal but acceptable if the desired transparency is not too high.

Whatever the nature of the basic polymer components of the hydrogel-forming polymeric absorbent gelling materials, such materials will in general be slightly crosslinked. Crosslinking serves to render the hydrogel-forming polymer gelling materials substantially water-insoluble, and cross-linking thus in part determines the gel volume and extractable polymer characteristics of the hydrogels formed from these polymeric gelling materials. Suitable crosslinking agents are well known in the art and include, for example, those described in greater detail in U.S. Patent 4,076,663 (Masuda et al), issued February 28, 1978. Preferred crosslinking agents are the di- or polyesters of unsaturated mono- or polycarboxylic acids with polyols, the bisacrylamides and the di- or triallyl amines. Other preferred crosslinking agents are N,N'-methylenebisacrylamide, trimethylol propane triacrylate and triallyl amine. The crosslinking agent can generally constitute from about 0.001 mole percent to 5 mole percent of the resulting hydrogel-forming polymer material. More preferably, the crosslinking agent will constitute from about 0.01 mole percent to 3 mole percent of the hydrogel-forming polymeric gelling material.

The slightly crosslinked, hydrogel-forming polymeric gelling materials are generally employed in their partially neutralized form. For purposes of the present invention, such materials are considered partially neutralized when at least 25 mole per-cent, and preferably at least 50 mole percent of monomers used to form the polymer are acid group-containing monomers that have been neutralized with a salt-forming cation. Suitable salt-forming cations include alkali metal, ammonium, substituted ammonium and amines. This percentage of the total monomers utilized which are neutralized acid group-containing monomers is referred to herein as the "degree of neutralization."

While these absorbent gelling materials have typically been disclosed in the prior art in granular form, it is possible in the context of the present invention that the absorbent gelling material is in a non-granular form for example as macrostructures such as fibers, sheets or strips. These macrostructures can be prepared by forming the particulate absorbent gelling material into an aggregate, treating the aggregated material with a suitable crosslinking agent, compacting the treated aggregate to densify it and form a coherent mass, and then curing the compacted aggregate to cause the crosslinking agent to react with the particulate absorbent gelling material to form a composite, porous absorbent macrostructure. Such porous, absorbent macrostructures are disclosed, for example, in U.S. Patent 5,102,597 (Roe et al), issued April 7, 1992.

d. Optional Fibrous Layer

An optional component for inclusion in the absorbent cores according to the present invention is a fibrous layer adjacent to, and typically underlying the storage layer. This underlying fibrous layer would typically provide the same function as the secondary fluid distribution layer.

e. Other Optional Components

The absorbent cores according to the present invention can include other optional components normally present in absorbent webs. For example, a reinforcing scrim can be positioned within the respective layers, or between the respective layers, of the absorbent cores. Such reinforcing scrims should be of such configuration as to not form interfacial barriers to fluid transfer, especially if positioned between the respective layers of the absorbent core. Given the structural integrity that usually occurs as a result of thermal bonding, reinforcing scrims are usually not required for the absorbent structures according to the present invention.

Another component which can be included in the absorbent core according to the invention and preferably is provided close to or as part of the primary or secondary fluid distribution layer are odor control agents. Typically active carbon coated with or in addition to other odor control agents, in particular suitable zeolite, silica or clay materials, are optionally incorporated in the absorbent core.

Physical characteristics of absorbent cores

Absorbent cores are usually non extensible and non-elastic, however, they can be rendered extensible and depending on the selected materials can also be made to have elastic characteristics. The term "extensible" as used hereinafter refers to a structure which under external forces such as those occurring during use extends in the direction of the forces or in the direction of a component of the forces in cases where only mono directional extensibility is provided.

The term "elastic" as used herein refers to extensible structures which return at least partially to their initial state after the forces causing the extension seize to be excerpted. Absorbent cores can be corrugated or pleated in one or several directions to provide a certain extensibility while selection of elastic fibers for the structure can provide elasticity.

The absorbent cores should preferably be thin. A thickness of less than 5 mm, preferably less than 3 mm and even more preferable between 0.8 and 1.8 mm is desirable such that the resulting articles can also have a low thickness.

Non-limiting examples of panty liners and sanitary napkins which may be provided with the blood detection composition include those manufactured by The Procter & Gamble Company of Cincinnati, Ohio as: ALWAYS® ALLDAYS® Pantiliners with DriWeave® manufactured according to U.S. Patents 4,324,246; 4,463,045; and 6,004,893; ALWAYS® Ultrathin Slender Maxi with Wings manufactured according to U.S. Patents 4,342,314, 4,463,045, 4,556,146, B1 4,589,876, 4,687,478, 4,950,264, 5,009,653, 5,267,992, and Re. 32,649; ALWAYS® Regular Maxi; ALWAYS® Ultra Maxi with Wings; ALWAYS® Maxi with Wings; ALWAYS® Ultra Long Maxi with Wings; ALWAYS® Long Super Maxi with Wings; and ALWAYS® Overnight Maxi with Wings.

Non-limiting examples of interlabial devices which may be provided with a blood detection composition are described in U.S. Patents 5,762,644; 5,885,265; 5,891,126; 5,895,381; 5,916,205; 5,951,537; 5,964,689; 5,968,026; Des. 404,814; and Des. 413,669.

Non-limiting examples of tampons which may be provided with blood detection composition and applicators therefor, are described in U.S. Patents 4,726,805; 4,846,802; 4,960,417; 5,087,239; 5,279,541; 5,346,468; 5,348,534; 5,531,674; and 5,566,435. In addition, the blood detection composition could also be placed on a digitally insertable tampon.

Blood Detection Composition

The blood detection composition according to the present invention provides at least one sensor for the detection of blood. As used herein, the term "sensor" is defined as a component comprising one or more reactive means

being adapted to detect one or more target substances (also referred to as analytes) such as microorganisms or related (bio-)molecules (e.g., an enzyme sensor, organella sensor, tissue sensor, microorganism sensor, immunosensor, and chemical or electrochemical sensor), additionally having the capability to provide a signal of said detection to the wearer, caretaker, or an actuator. When referring to blood herein a typical component of blood, such as hemoglobin or iron, can of course also be used as analyte. The term "reactive" is defined as having the capability to selectively interact with such target substances.

There are 2 categories of sensors which have different sensitivity: biosensors and chemical-/electro-chemicall sensors. Generally biosensors function by providing a means of specifically binding, and therefore detecting, a target biologically active analyte. In this way, the biosensor is highly selective, even when presented with a mixture of many chemical and biological entities, such as vaginal discharge. Electrochemical and chemical sensors, on the other hand, which rely on chemically reactive means, generally do not have either the high selectivity or the amplification properties of biosensors but are highly reliable, inexpensive, i.e. useful for commodity products, and often very well established, i.e. proven to be save for use on human skin. Often the target analyte is a minor component of a complex mixture comprising a multiplicity of biological and other components. Thus, in many biosensor applications, detection of target analytes to the parts-per-billion, parts-per-trillion, or even lower levels is necessary.

According to the present invention the blood detection composition is a specifically stabilized chemical composition. The chemical composition comprises a color indicating component which provides a color change as a result of an oxidation reaction and is preferably selected from Gum Guaiac or tetra-methyl-benzidine or combinations thereof. As a second component the composition comprises as a stabilized oxidizing component a peroxide or a per-acid.

The oxidizing component (also referred to as oxidant) is stabilized to be insensitive to storage conditions usual in the context of the intended articles (e.g. in a warm and high humidity environment of a bathroom). Stabilization can be provided in 2 ways: physio-chemical stabilization by caging the oxidante onto a carrier. According to the present invention this carrier is provided by cyclo-dextrin. The cyclo-dextrin carries the peroxide in an aqueous phase (e.g. in the presence of high humidity) while maintaining the oxidative reactivity. An alternative to the physio-chemical stabilization is the chemical stabilization by preventing or reducing degradation due to radicals. According to the present invention this is achieved by the use of nitrone. Of course the use of both components together is also possible and does create an additional stabilizing effect.

If the oxidant is selected to be a per-acid it preferably is a epta-phtalimido-peroxy-hexanoic acid. The epta-phtalimido-peroxy-hexanoic acid also benefits from stabilization by caging but preferably can be stabilized by nitrone to block or reduce the degradation due to radicals. In this context nitrone functions as a radical scavenger and other radical scavengers can also be used. Of course in mixtures of hydro-peroxide and epta-phtalimido-peroxy-hexanoic acid also both stabilizer components need to be present.

The color indicator and the oxidizing material both are reactive primarily in aqueous solution. Hence they will start to react once they have dissolved in the vaginal discharges and are activated by the presence of blood. In order to accelerate and promote the dissolution it is preferred to include a tensioactive e.g a surfactant, or polyethylene-glycol or mixtures thereof, preferably polyethylene-glycol, in the blood detection composition. In a sanitary article the tensioactive material should preferably be located such that it is wetted first before the liquid reaches the 2 components.

A highly preferred composition comprises a combination of epta-phthalimido-peroxy-hexanoic acid and Gum Guaiac. The Gum Guaiac is a resin found from wood of Guaiacum officinale or Guaiacum santum (mainly found in Mexico or West India). Gum Guaiac is historically used as flavoring agent for food (and hence has a long record of save usage by humans) and is known for its ability to indicate the presence of blood or hemoglobin, especially in feces. According to the present invention the Gum Guaiac wood resin is preferred, however one or all of the active components, whether naturally or artificially derived, can be used in stead of the wood resin. The best known active components are guaiacol (OHC6H4OCH3, CAS 90-05-1), guaiaconic acid and (furo)-guaiacine.

If applied to an article the components can be applied by coating or spraying provided they are applied in solution. The solvent in this case should preferably be an organic solvent. However such solvent should evaporate at temperatures below 100 °C, unless the organic solvent can be selected to provide additional benefits to the article, such as a tensioactive as dissolution aide. If used in an absorbent article application of both components on the same layer can be done in an alternate pattern such as stripes, dots or different shapes. The detector components can be provided in discrete parts of a surface of a layer or as full surface coverage of the layer (both components or one alone). The components can be provided either one or both as powder, liquid or as components in an adhesive admixture for better coating.

Additional Detectors

In one particularly preferred embodiment of the present invention the composition (or if the composition is applied to an article the article) comprises in addition to the blood detector another separately activated and independently functioning sensor to detect a physiological component in bodily discharges.

Without limitation this will be exemplified in the following by detection of the approach of menstruation.

It is clear that the detection of blood in particular to allow prediction of menstruation cannot be considered to be one hundred percent accurate. First of all, the indicator itself needs to be provided with a high degree of accuracy for only detecting blood, i.e. it should be insensitive to other materials to which it is exposed. On the other hand, the sensitivity should be high to allow detection of low quantities of blood, i.e. prior to its visual recognition. These two competing interests need to be balanced.

Further the presence of (occult) blood is well known as an indication of the approach of menstruation. However also injuries or pathological situations may cause the presence of low levels of blood in vaginal discharges. It is therefore desirable to provide the sanitary article with an additional indicator providing a second signal of the approach of menstruation. Such a signal can be provided, for example, by the change of pH of the vaginal discharge within the days prior to menstruation. In addition or alternatively, hormones such as progesterone and/or estrogen can be used as additional indicators for the prediction of menstruation.

Most preferred in this context are pH sensors which can also be provided as a color change indicators. pH sensors are well known and are commercially available e.g. from The Merck Company, Darmstadt, Germany. A highly preferred pH sensor, having a well established safety profile in this context is carminic acid, which is used as a food dye, but undergoes a color change in the range between pH 4 and pH 7. Carminic acid is a tricyclic compound which has the compound formula C22-H20-O13.

Regardless of which additional sensors are used, if they are provided as color change indicators together with the color indicator providing blood detection they will create a mixed output signal in the form of a multicolor indication. That

can be a mixed color indication or it can be provided separate and individually detectable but functioning togethrer as explained below.. For example, if Gum Guaiac, which provides a color change to blue is mixed with a pH sensor providing e.g. a color change to red, the mixed color sensor (blue and red) would need to turn purple in order to provide an indication with high accuracy and time proximity of the approach of menstruation. A different color change (such as only blue or only red) would indicate that either the menstruation is still some time away or that there is the potential of a health issue (a pH change alone can be indicative - but does not have to - of infections, while blood indication alone can - but does not have to - indicate a wound). For such changes the packaging of the composition (or the article if allied on an article) could include an instruction to the user to consider visiting a physician to medically evaluate whether any serious health issue (pathological situation) exists. Of course the absence of a color change would indicate that there is still time until the next menstruation.

In addition to the electrochemical sensors, to supplement the blood detector, the cyclic nature of the hormones of the menstrual cycle (i.e., the full 28 day cycle) make them particularly useful in understanding, the position of an individual during her cycle. This has historically been used in the assessment of fertility, but the use according to the present invention goes beyond current uses of hormones to predict ovulation and pregnancy. For example, progesterone peaks and then drops just prior to menstruation. Estrogen also declines just prior to menstruation. Thus, in combination with other predictors, such as blood detection or pH indication, assay for either of these two hormones will allow reliable prediction of the onset and the presence of menstruation. The timing of the peak of these hormones, along with their subsequent drop, allows a highly accurate marking of the time before menstruation.

The only potential drawback of such hormone indication is the associated cost and complexity. The lack of simple visualization makes their use in mass produced bulk articles not very attractive. Hence the use of hormone detection in

order to predict menstruation is preferably provided in conjunction with blood detection and/or pH detection to improve the accuracy of such predictions in the form of a completely separate detection system.

Use of hormones may also be developed for other points of interest in the cycle. Follicle Stimulating Hormone (FSH) exhibits a peak about one week prior to ovulation, giving more advance timing for pregnancy planning than assays for the luteinizing hormone, which exhibits a sharp peak at the time of ovulation. Two to three days of fertility may be missed when relying only on assay of the luteinizing hormone. Thus, in a diagnostic for ovulation herein, it is highly preferred to measure for both the Follicle Stimulating Hormone and the luteinizing hormone along with estrogen.

A rise in Follicle Stimulating Hormone to a near constant amount signals the approach of menopause. This may be of use in planning healthy approaches to menopause, such as Hormone Replacement Therapy, nutritional changes, and checks for osteoporosis.

The composition according to the present invention can be provided with several additional sensor and detector systems which allow e.g. indications or predictions of health related issues of the individual. Such additional sensor systems are primarily useful for sanitary articles which are used in a care taker situation or if the composition is in the form of a spray or liquid. In general such additional systems or biosensors comprise a recognition element, or molecular recognition element, that provides detection for a particular analyte. The recognition element may be a biologically derived material such as an enzyme or sequence of enzymes; an antibody; a membrane receptor protein; DNA; an organelle, a natural or synthetic cell membrane; an intact or partial viable or nonviable bacterial, plant or animal cell; or a piece of plant or mammalian tissues, and generally functions to interact specifically with a target analyte. The

recognition element is responsible for the selective recognition of the analyte and creates a physical-chemical signal that provides the basis for the output signal.

Biosensors may include biocatalytic biosensors, and bioaffinity biosensors. In biocatalytic biosensor embodiments, the bio-recognition element is "biocatalytic" and may comprise an enzyme, organelle, piece of plant or mammalian tissue, or whole cells, the selective binding sites "turn over" (i.e., can be used again during the detection process), resulting in a significant amplification of the input signal. Biocatalytic sensors such as these are generally useful for real-time, continuous sensing.

Bioaffinity sensors are generally applicable to bacteria, viruses, and toxins and include chemoreceptor-based biosensors and/or immunological sensors (i.e. immunosensors). Chemoreceptors are complex biomolecular macroassemblies responsible, in part, for a viable organism's ability to sense chemicals in its environment with high selectivity. Chemoreceptor-based biosensors comprise one or more natural or synthetic chemoreceptors associated with a means to provide a signal (visual, electrical, etc.) of the presence or concentration of a target biological analyte. Chemoreceptors may include whole or partial nerve bundles (e.g., from antennae or other sensing organs) and/or whole or partial natural or synthetic cell membranes. On the other hand, the bio-recognition elements of immunosensors are generally antibodies. Antibodies are highly specific and can be made toward bacteria, viruses, fragments of microorganisms (e.g., bacterial cell walls, parasite eggs or portions thereof, etc.), and large biomolecules. Suitable antibodies may be monoclonal or polyclonal. In any case, bioaffinity biosensors are generally irreversible because the receptor sites of the biosensor become saturated when exposed to the target biological analyte. In certain embodiments biocatalytic and bioaffinity biosensors may be combined. Biocatalytic and bioaffinity biosensor systems are described in more detail in Journal of Chromatography, 510 (1990) 347-354 and in the Kirk-Othmer Encyclopedia of Chemical Technology, 4th ed. (1992), John Wiley & Sons, NY.

The biosensors of the present invention preferably also detect biologically active analytes related to impending (i.e., future presentation of symptoms is likely) or current human systemic disease states, including pathogenic bacteria, parasites, viruses, fungi such as Candida albicans, antibodies to pathogens, and/or microbially produced toxins. Additionally, the biosensor may target biologically active analytes related to impending or current localized health issues, such as stress proteins (e.g., cytokines) and IL-1α (interleukin 1-alpha) that may precede the clinical presentation of skin irritation or inflammation. In preferred embodiments, the biosensor functions as a proactive sensor, detecting and signaling the wearer or caretaker of the impending condition prior to the presentation of clinical symptoms. This allows time to administer prophylactic or remedial treatments to the wearer which can significantly reduce, if not prevent, the severity and duration of the symptoms. Further, the biosensor by detecting the presence of a target biological analyte in the wearer's bodily waste, may detect residual contamination on a surface, such as skin, in contact with the biosensor, and provide an appropriate signal.

The signal generated by the recognition element or elements is communicated visually to the wearer or caretaker, e.g. via a color change visible to the human eye. The signal may be qualitative (e.g., indicating the presence of the target biological analyte) or quantitative (i.e., a measurement of the amount or concentration of the target biological analyte). In any case, the signal is preferably durable i.e., stable and readable over a length of time (typically at least of the same magnitude as the usage period of the article). Further, the sensor may be adapted to detect and/or signal only concentrations of the target biological analyte above or below a predefined threshold level (e.g., in cases wherein the target biological analyte is normally present in the bodily waste).

As described above, the target analyte that the biosensors of the present invention are adapted to detect is pathogenic microorganisms such as the

pathogenic microorganisms implicated in human gastrointestinal diseases, especially those resulting in diarrhea. It has been found that severe chronic diarrhea may result in weight loss and permanent physical and mental retardation. A non-limiting list of pathogenic bacteria that the biosensor 60 may detect include any of the various pathogenic strains of *Escherichia coli* (commonly known as *E. Coli*); *Salmonella* strains, including *S. typhi*, *S. paratyphi*, *S. enteriditis*, *S. typhimurium*, and *S. heidelberg*; *Shigella* strains such as *Shigella sonnei*, *Shigella flexneri*, *Shigella boydii*, and *Shigella dysenteriae*; *Vibrio cholerae*; *Mycobacterium tuberculosis*; *Yersinia enterocolitica*; *Aeromonas hydrophila*; *Plesiomonas shigelloides*; *Campylobacter* strains such as *C. jejuni* and *C. coli*; *Bacteroides fragilis*; and *Clostridia* strains, including *C. septicum*, *C. perfringens*, *C. botulinum*, and *C. difficile*. A non-limiting example of a commercially available biosensor adapted to detect *E. coli* is available from AndCare, Inc. of Durham, NC, as test kit #4001. ABTECH, Scientific, Inc., of Yardley, PA offers "bioanalytical biotransducers", available as BB Au-1050.5-FD-X, which may be rendered biospecific (for microorganisms or other target biological analytes as described herein) by covalently immobilizing polypeptides, enzymes, antibodies, or DNA fragments to their surfaces. Other suitable microbial biosensors are described in US Patents 5,869,272 (gram negative organisms); 5,795,717 (*Shigella*); 5,830,341; 5,795,453; 5,354,661; 5,783,399; 5,840,488; 5,827,651; 5,723,330; and 5,496,700.

The target analytes that the biosensors of the present invention are adapted to detect may also be viruses. These may include diarrhea-inducing viruses such as rotavirus, or other viruses such as rhinovirus and human immunodeficiency virus (HIV). An exemplary biosensor adapted to detect HIV is described in US Patents 5,830,341 and 5,795,453, referenced above.

In alternative embodiments, the target analytes that the biosensors of the present invention are adapted to detect may also be parasites, especially those which inhabit the gastrointestinal tract during some point in their life-cycle. Such

parasites may include protozoans, worms, and other gastrointestinal parasites. Other examples of parasites which may be detected include *entamoeba histolytica* (which cause amoebic dysentery), *trypana cruzi* (which causes Chagas disease), and *plasmodium falciparum*.

In yet other embodiments, the target analytes the biosensors of the present invention are adapted to detect fungi such as *Candida albicans*. In addition to pathogenic bacteria, certain beneficial colonic bacteria may be detected and/or measured as a health indicator, such as *Bifidobacteria* and *Lactobacillus* strains.

The target analytes that the biosensors of the present invention are adapted to detect may also be proteins or antigens related to skin distress. Preferably, these analytes are detectable on or at the skin surface, preferably prior to the presentation of clinically observable skin irritation. These may include stress proteins such as cytokines, histamine, and other immune response factors including interleukins (such as IL-1α, IL-2, IL-3, IL-4, and IL-8) and interferons (including interferons a and g). Again, these are preferably detectable by the biosensor 60 prior to the onset of clinically observable redness, irritation, or dermatitis. Additionally, the biosensors of the present invention may be adapted to detect enzymes, or other biological factors, implicated in skin irritation (e.g., diaper dermatitis), including tryspin, chymotrypsin, and lipase.

The biosensors of the present invention may also comprise bio-recognition systems, including enzymes or binding proteins such as antibodies immobilized onto the surface of physico-chemical transducers. For example, a specific strain of bacteria may be detected via biosensors employing antibodies raised against that bacterial strain. Alternatively, a target bacteria may be detected by a bio-recognition element (including antibodies and synthetic or natural molecular receptors) specific to extracellular products of the target bacteria, such as toxins produced by that strain (e.g., *E. coli*). Exemplary enzyme electrodes that may be used to detect phenols (e.g. in urine or feces) include tyrosinase based

electrodes or polyphenol oxidase enzyme electrodes described in U.S. Patent No. 5,676,820 entitled "Remote Electrochemical Sensor," issued to Joseph Wang et al. on October 14, 1997 and U.S. Patent No. 5,091,299 entitled "An Enzyme Electrode For Use In Organic Solvents," issued to Anthony P. F. Turner et al. on February 25, 1992, respectively

In any of the foregoing examples, the specific microorganism may be directly detected or may be detected by binding a toxin, enzyme, or other protein produced by the organism or an antibody, such as a monoclonal antibody, specific to the organism. Exemplary biosensors adapted to detect proteolytic enzymes described in US Patent 5,607,567 and toxins in US Patents 5,496,452; 5,521,101; and 5,567,301.

The biosensor of the present invention may comprise one or more "proactive sensors". This is especially useful in embodiments where the detection of the target biologically reactive analyte precedes the onset of clinically observable health symptoms. As used in this application, the term "proactive sensor" refers to a sensor that is capable of detecting changes or signals on the body of the wearer (i.e., skin) or in the waste, i.e., inputs, that directly relate or, at a minimum, correlate to the occurrence of an impending or potential health or skin related even. Proactive sensors may respond to one or more specific inputs as described above.

A proactive sensor may detect an impending event or detect a parameter that directly relates, or at a minimum correlates to the occurrence of an impending event, particularly a systemic or skin health event or condition (i.e., the presentation of clinically observable indications or symptoms). An impending event that may be detected or predicted by a proactive sensor of the present invention may include diarrheal disease, skin irritation or rash (including candidiasis), and/or other types of illness or medical conditions of the wearer such as a parasitic infestation. The detected biological analyte may be one or

more steps removed from the actual presentation of clinical symptoms. For example, the biosensor may detect potential precursors to the above conditions (e.g., fecal contamination of the skin that may precede the elicitation of stress proteins which may, in turn, precede clinically observable skin irritation. A parameter that correlates to an event is any measurable input, signal such as one or more of the potential inputs listed above, that correlates with the occurrence of the event within the frame of reference of the system (i.e., a signal caused by the waste or the wearer). Proactive sensors in an article may measure one or more different inputs in order to predict an event. For example, the proactive sensor may monitor for *Candida albicans* in vaginal discharges and residual colonic bacteria on the skin (i.e., detecting residual contamination) both of which are signals that may precede skin irritation.

In biosensor embodiments wherein the bio-recognition element does not produce an easily visible signal (e.g., a color change), the biosensor may include a transducer in communication with the bio-recognition element in order to convert the physico chemical signal from the bio-recognition element into a usable signal to the wearer, caretaker, or component of the article (e.g., and actuator). Exemplary transducers may include electrochemical transducers (including potentiometric, amperometric, and conductimetric transducers), optical transducers (including fluorescence, bioluminescence, total internal reflective resonance, and surface plasmon resonance), thermal transducers, and acoustic transducers, as known in the art. A power source, such as a miniature 3 volt watch battery or printed thin film lithium battery, may be connected with the biosensor to provide any required power.

CLAIMS

1.) Stabilized detection composition for providing a visual signal of the detection of blood in liquids, such as bodily fluids of mammalian origin or aqueous solutions thereof, which blood is not discernible by normal visual inspection by the human eye,
said blood detection composition comprising
- an oxidisable color indicator, and either one or both of the following group
- a peroxide, and as a stabilizer for said peroxide a component selected from cyclo-dextrin or nitrone or combinations thereof; or
- a per-acid, and as a stabilizer for said per-acid nitrone.

2.) Composition according to claim 1 characterized in that said oxidisable color indicator is selected from the group consisting of Gum Guaiac, tetra-methyl benzidine or combinations thereof, preferably Gum Guaiac.

3.) Composition according to any of the preceding claims characterized in that said peroxide is a hydro-peroxide.

4.) Composition according to any of the preceding claims characterized in that said per-acid is a epta-phtalimido-peroxy-hexanoic acid.

5.) Composition according to any of the preceding claims characterized in that said composition is in a liquid form, preferably as a solution in an organic carrier.

6.) Composition according to any of the preceding claims 1 - 4 characterized in that said composition is in particulate form.

7.) Composition according to any of the preceding claims characterized in that it further comprises a tensioactive material.

8.) Article for visual blood detection of a quantity of blood in liquids, which blood is visually not discernible, said article comprising a carrier material on which a detection composition according to claim 1 has been applied.